

Table 1: Overview of modelling approaches used to assess the association between time-specific exposure variables and reproductive outcomes.

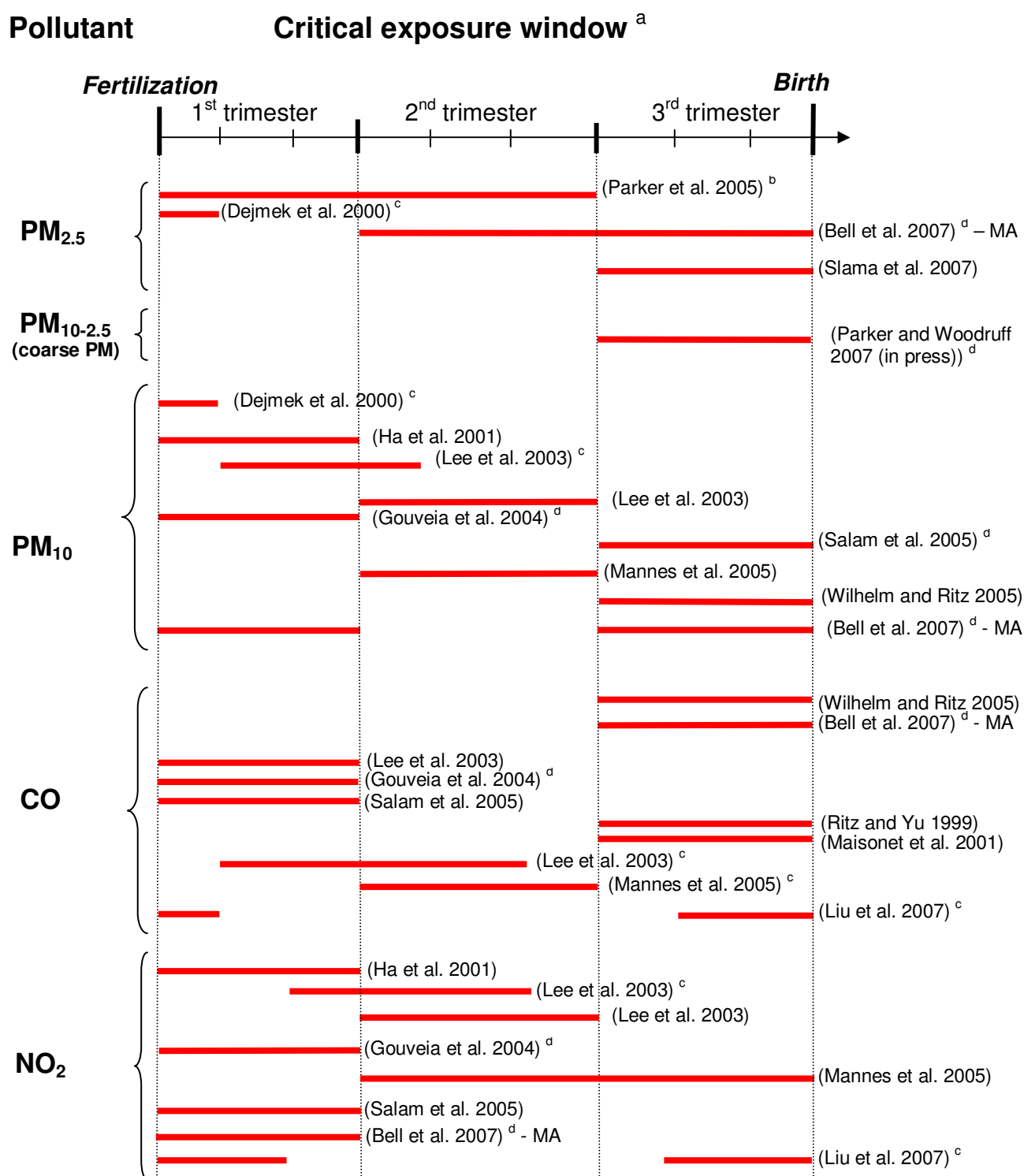
Principle	Coding of exposure term $\beta E^{a,b}$	Comment	Main drawbacks
1. One exposure variable at a time	$\beta x E_{(\text{trimester } j)}$, where $j=1, 2 \text{ or } 3$	Repeat the approach for each time-specific exposure variable	The estimated effect of each time specific variable is potentially confounded by that of the other variables.
2. Stratify on season of conception	$\beta x E_{(\text{whole pregnancy})}$	Estimate separately for pregnancies conceived during each season	Seasonal patterns in exposure may vary from year to year or across locations.
3. Mutually-adjusted exposure variables	$\beta_1 x E_{(\text{trimester } 1)} +$ $\beta_2 x E_{(\text{trimester } 2)} +$ $\beta_3 x E_{(\text{trimester } 3)}$	One single regression model	If some time-specific exposure variables are strongly correlated then the resulting estimates may be unstable.
4. Two-step approach using residual exposure (Bell et al. 2007)	$\beta_1 x E_{(\text{trimester } 1)} +$ $\beta_2 x \text{Residual } E_{(\text{trimester } 2)} +$ $\beta_3 x \text{Residual } E_{(\text{trimester } 3)}$	Residual mean corresponds to the residuals of a linear model in which mean exposure during a given trimester is regressed over exposure during the previous trimesters.	

^a All approaches rely on a regression model written $g[E(Y)] = \alpha + \beta E + \gamma Z$, where Y is the reproductive outcome, g the link function

5 (e.g. logistic), E the vector corresponding to exposure specified in the table and Z the vector of adjustment variables, with β and γ being the corresponding parameter vectors. We assumed for simplicity that each pollutant was considered separately.

^b Examples are given for trimester specific exposure variables, but month-specific variables have also been used (e.g. Lee et al. 2003).

Figure 1: Time windows corresponding to the highest estimated effect of air pollutants on fetal growth reported in published studies.



^a Only studies reporting the associations between all trimester-specific (or month-specific) maternal exposures to air pollutants during pregnancy on either birthweight or small for gestational age/IUGR births have been retained. For each study, the effect estimate corresponding to the time window with the highest relative risk is indicated by a horizontal bar (thus not all significant associations are reported here). If the exposure windows with the two highest excess risks (defined as relative risk minus 1) differed by less than 10% then both windows were reported.

MA: Indicates studies in which the trimester-specific exposure variables were mutually adjusted for in a single regression model. Results otherwise correspond to models in which each trimester- or month-specific exposure variable was entered separately.

^b Also adjusted for CO levels.

^c Analysis performed using month-specific exposure variables.

^d Birthweight was analyzed as a continuous outcome adjusted for gestational age. In other studies, birthweight was analyzed as a binary outcome.

References (supplemental material)

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